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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
4161	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,045	LEPHART ET AL.	
	Examiner	Art Unit	
	PAUL ZAREK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/02/2005, 03/28/20007, 08/08/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-22 have been canceled by the Applicant. Claim 23-42 were added on 04/28/2005. Claims 23-42 are currently pending. This is the first Office Action on the merits of the claim(s).

Priority

2. Applicant's claim for the benefit of a prior-filed international application PCT/US03/34441 (filed on 10/29/2003) which claims the benefit of US provisional application 60/422,469 (filed on 10/29/2002) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 10/29/2002.

Claim Rejections - 35 USC § 112 (1st paragraph)

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating or reducing the physiological and pathophysiological conditions mediated by androgens comprising administration of equol, does not reasonably provide enablement for enhancing the physiological and pathophysiological conditions mediated by androgens comprising administration of equol. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (MPEP § 2164.01(a)) All Wands factors were carefully considered and the relevant factors are discussed herein:

a. *The breadth of the claim*: Claims 23-29 are drawn to a method of modulating a physiological and pathophysiological condition mediated by androgens comprising the administration of enantiomeric equol. Modulate can be defined as adjusting or adapting to a certain proportion to a certain measure or proportion (American Heritage Dictionary, 4th Ed.). Therefore, Claims 23-29 can reasonably be interpreted as a method to make the physiological and pathophysiological condition either better or worse.

b. *Nature of the invention*: The nature of the invention is a method of alleviating an androgen-mediated illness through the administration of enantionmeric equol;

c. *The state of the prior art*: It is generally accepted that the purpose of treatment is to speed a subject's recovery from an illness. Methods that make the subject more ill or sick are not desired.

d. *Amount of direction provided by the inventor*: Applicant alleges that administration of equol could be an effective treatment to prevent multiple diseases, including prostate cancer (paragraph 0128), Alzheimer's disease (paragraph 0129), obesity (paragraph 0136), and high cholesterol, (paragraph 0138);

e. *Existence of working examples*: All working examples disclose methods of treating animals to allow recovery from induced androgen-mediated conditions. Administration of enantiomeric equol were effectively treated the androgen-mediated illness. No examples were provided in which administration of enantiomeric equol made the animal more sick; and,

f. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: The nature of the invention is a method of treatment such that the subject would recover from an androgen-mediated, physiological and pathophysiological condition. Indeed, such an effect would be desirable. The instant specification provides no guidance for a method of making a physiological and pathophysiological condition worse by the administration of enantiomeric equol. The prior art does not make up for this deficit. Therefore, undue experimentation would be required to use the invention commensurate with the scope of the rejected claims.

6. Claims 30-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating an androgen-related condition comprising administration of equol, does not reasonably provide enablement for preventing an androgen-related condition comprising administration of equol. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

7. All Wands factors were carefully considered and the relevant factors are discussed herein:

a. *The breadth of the claim*: Claims 30-44 are drawn to a method of both treating and preventing an androgen-related disease comprising administration of enantiomeric equol. Examples of said androgen-related disease include, but are not limited to, Alzheimer's disease, high cholesterol, obesity, and prostate cancer;

b. *The state of the prior art*: Many of the androgen-related diseases are multifactorial and are caused by combinations of environmental factors, life style, diet, and genes. The multifactorial nature of these diseases suggest that prevention, if even possible, would require changes in life style, diet and environment;

c. *Amount of direction provided by the inventor*: Applicant alleges that administration of equol could be an effective treatment to prevent multiple diseases, including prostate cancer (paragraph 0128), Alzheimer's disease (paragraph 0129), obesity (paragraph 0136), and high cholesterol, (paragraph 0138);

d. *Existence of working examples*: All working examples are drawn to treatment methods in which equol or dietary phytoestrogen was administered following the induction of the condition to be treated. No examples were given for prevention of any diseases; and,

e. Quantity or experimentation needed to make or use the invention based on the content of the disclosure: Applicant has provided no direction that would enable one of ordinary skill in the art to prevent an androgen-mediated disease comprising administration of enantiomeric equol. Many of the diseases claimed to be prevented are multifactorial in nature and are unable to be prevented through the administration of a single compound. Any attempt to do so would require unpredictable and unguided

research. Therefore, Claims 30-44 are not enabled by the instant specification for prevention of an androgen-mediated disease.

Claim Rejections - 35 USC § 112 (2nd paragraph)

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 27, 28, 32, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 27, 28, 32, and 33 are drawn to a method of treatment comprising the administration of a composition comprising essentially the R-equol (Claims 27 and 32) or S-equol (Claims 28 and 33) enantiomer. The rejected claims are indefinite because neither the claims nor the instant specification disclose the meaning of "essentially," therefore the rejected claims are rendered indefinite.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 23-26, 30, 31, and 35-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelly et al. (International Application No. WO 98/08503, 1998, provided in IDS).

12. Claims 23-26, 30, 31, and 35-44 of the instant application are drawn to methods of modulating an androgen-mediated condition (Claims 23-26), treating or preventing an androgen-mediated disease (Claims 30, 31 and 35-37), or treating or preventing a combination androgen- and estrogen-mediated condition (Claims 38-41). Androgen-mediated diseases descend from physiological or pathophysiological conditions mediated by androgen, so a treating an androgen-mediated disease necessarily modulates an androgen-mediated condition. Claims 25, 35, and 40 limit the oral composition to comprising at least 1 mg enantiomeric equol. Claims 26, 36, and 41 limit the topical composition to comprising at least 0.1% enantiomeric equol. Claims 38-41 limit the method to treating or preventing a combination of androgen- and estrogen-mediated conditions wherein the R-equol binds to 5α-dihydrotestosterone and S-equol binds to both 5α-dihydrotestosterone and the estrogen receptor. Claims 37 and 44 limit the composition administered to be free of any other androgen-binding component.

Kelly, et al., teach that equol (compound 10) can be used to treat prostate cancer (Example 6b), elevated LDL levels (Example 6c), acne (Example 7), and male-pattern baldness (Example 11), which are all androgen-mediated diseases. Kelly, et al., further teach an oral composition, wherein the daily dose is between 0.1 mg- 2.0 g (pg 9, lines 15-16) or a topical composition wherein the equol concentration is between 0.1%-0.5% (pg 11, lines 19-24). The composition taught by Kelly, et al., need not contain another androgen-binding component. R-equol inherently binds to 5α-dihydrotestosterone, while S-equol inherently binds to both 5α-dihydrotestosterone and the estrogen receptor. That these characteristics of R- and S-equol were

not known at the time of invention does not render an invention novel (MPEP § 2112). "Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Therefore, Kelly, et al., anticipates all the limitations of the rejected claims.

13. Claims 23, 24, 28, 30, 31, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorbach (International Application No. WO 98/25588, provided in IDS) as evidenced by Setchell, et al. (American Journal of Clinical Nutrition, 2005, provided in IDS).

14. Claims 23, 24, 30, and 31 are discussed above. Claims 28 and 33 of the instant application depend upon Claims 23 and 30, respectively, and limit the composition to comprising essentially the S-equol enantiomer. Gorbach teach a method of treating Alzheimer's disease comprising administration of isoflavonoids (abstract). Setchell, et al., teach that the exclusive product of isoflavones is S-equol (abstract). The isoflavonoids administered by Gorbach necessarily and inherently were converted to S-equol prior to mediating their Alzheimer's disease-treating effect. Therefore, Gorbach anticipates all the limitations of the rejected claims.

15. Claims 23, 24, 27, 30, 31, and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Setchell and Cole (US PreGrant Publication No. 2004/0235758, provided in IDS, claiming priority to 60/398,270, filed on 07/24/2002).

16. Claims 23, 24, 30, and 31 are discussed above. Claims 27 and 32 of the instant application, which depend upon Claims 23 and 30, respectively, are drawn to methods of treating wherein the composition is comprised of essentially R-equol. Setchell and Cole teach a method of administering R-equol to treat Alzheimer's disease (paragraph 0142), high cholesterol

(paragraph 0145, cardiovascular disease (paragraph 0147), and prostate cancer (paragraph 0151), among others. Therefore, Setchell and Cole anticipate all the limitations of the rejected claims.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 23, 29, 30, 34, 38, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kelly, et al., in view of Luk, et al. (Journal of Natural Products, 1983, provided in IDS).

20. Claims 23, 30, and 38 are discussed above. Claims 29, 34, 42, and 43 of the instant application, which depend upon Claims 23, 30 and 38, respectively, are drawn to a method of treatment of androgen-mediated (Claims 29 and 34) or androgen- and estrogen-mediated (Claims 42 and 43) diseases comprising the administration of a non-racemic mixture of R- and S-equol.

Kelly, et al., discussed above, teach that equol (compound 10) can be used to treat prostate cancer (Example 6b), elevated LDL levels (Example 6c), acne (Example 7), and male-pattern baldness (Example 11), which are all androgen-mediated diseases. Kelly, et al., does not teach a non-racemic mixture of equol for treatment of androgen-mediated diseases. Luk, et al., teach that both R- and S-equol were known (pg 853, lines 1-3). A racemic mixture is defined as a mixture consisting of exactly 50% of each enantiomer. A mixture containing 51% R-equol and 49% S-equol would be considered a non-racemic mixture. One of ordinary skill in the art would reasonably predict that delicately altering the 50:50 ratio of R- to S-equol of a racemic mixture to a non-racemic mixture consisting of a 51:49 ratio of R- to S-equol would maintain the therapeutic effect of the racemate. Such subtle alterations would constitute routine optimization, which is not considered a patentably distinguishing feature (MPEP § 2144.05). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to use a non-racemic mixture of the racemate taught by Kelly, et al.

Conclusion

21. No claims are Allowed

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, PATRICK NOLAN can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Ashwin Mehta/
Primary Examiner, Technology Center 1600